AMENDMENTS AND UPDATES TO
HUMAN GENE TRANSFER PROTOCOLS
RECOMBINANT DNA ADVISORY COMMITTEE MEETING
JUNE 28-29, 2000

From mid-March to early June 2000	Protocols: 9709-210 9804-243 9907-327/328/329 9812-271 9901-280 9908-333 9910-346 9912-366 0002-388 0002-391	These ten protocols had a total number of 36 new sites/investigators added. Protocol 9901-280 had eight new sites/investigators. Protocol 9912-366 had six new investigators/sites added. Protocols 9804-243, 9910-346, 0002-388, and 0002-391 each had four new investigators/sites added. The remaining protocols had three or fewer new investigators/sites added.
From mid-March to early June 2000	Protocols: 9212-036 9306-049 9312-067 9409-091 9412-094 9701-172 9705-189 9706-194 9803-241	Notification has been received that these nine protocols are now closed and/or the IND has been withdrawn.
February 2, 2000 (letter	9409-085	**Evaluation of Repeat Administration of a Replication Deficient,**

date)	Crystal	**Recombinant Adenovirus Containing the Normal Cystic Fibrosis Transmembrane Conductance Regulator cDNA to the Airways of Individuals with Cystic Fibrosis** **Update:** Due to a lack of resources, life-long follow-up will not be performed. Patients that have not been lost to follow-up have been informed of this.

February 2, 2000	9509-125 Crystal *et al.*	**A Phase I Study of Direct Administration of a Replication-Deficient Adenovirus Vector Containing the E. coli Cytosine Deaminase Gene to Metastatic Colon Carcinoma of the Liver in Association with the Oral Administration of the Pro-Drug 5-Fluorocytosine** **Update:** Due to a lack of resources, life-long follow-up will not be performed. Patients that have not been lost to follow-up have been informed of this.
February 10, 2000	9908-336 Smith	**Post-Transplant Infusion of Fibronectin-Assisted, Retroviral-Mediated Gene-Marked and Ex Vivo Expanded CD34+ Placental and Umbilical Cord Blood Cells** **Amendments:** Administrative and clinical clarifications were made.
February 10 and 17, 2000	9712-223 and 9712-224 Brenner	**Phase I Study of Chemokine and Cytokine Gene Modified Allogeneic Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using a Retroviral Vector** **Phase I Study of Chemokine and Cytokine Gene Modified Autologous Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using an Adenoviral Vector** Both protocols have been amended to allow for a maximum dose for Lptn cells to be 10^8.
February 11 to March 10, 2000	9712-224 and 9905-319 Brenner	**Phase I Study of Chemokine and Cytokine Gene Modified Autologous Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using an Adenoviral Vector** **Treatment of High Risk Acute Leukemia with CD40 Ligand and IL-2 Gene Modified Autologous Bone Marrow Fibroblasts and Tumor Cells** **Updates:** Concerning the possible contamination of viral vector with HIV and Hepatitis C. This issue was also reported by Dr. Bowman at St. Jude's (copy of Dr. Bowman's letter was included in the March 2000 RAC meeting material).
February 14 to April 26, 2000	9701-173 Croop	**A Pilot Study of Dose Intensified Procarbazine, CCNU, Vincristine (PCV) for Poor Prognosis Pediatric and Adult Brain Tumors Utilizing Fibronectin-Assisted, Retroviral-Mediated Modification of CD34+ Peripheral Blood Cells with O^6-Methylguanine DNA Methyltransferase** **Updates:** Several letters of correspondence during this time period relating to the possible presence, detected by PCR, of replication competent retrovirus in transduced CD34+ cells. New patients were not enrolled onto this study after the positive PCR result. During this time the live virus assay (S+L-) continued to give reliable results and was used to monitor blood of all previously treated patients. It was determined that the positive PCR result was due to contaminating DNA and not due to replication competent retrovirus.
February 17, 2000	9802-237 Roessler	**Molecular Synovectomy by In Vivo Gene Transfer: A Phase I Trial** **Amendment:** Ambiguous language in the inclusion and exclusion criteria was

		modified.
February 18, 2000	9701-172 Cornetta and Abonour	**High Dose Carboplatin and Etoposide Followed by Transplantation with Peripheral Blood Stem Cells Transduced with the Multiple Drug Resistance Gene in the Treatment of Germ Cell Tumors - A Pilot Study** **Update:** To date 12 patients have been enrolled (accrual goal is 15). One of the 12 did not mobilize sufficient number of cells to meet the eligibility requirements. (This one patient received a tandem transplant of transduced and non transduced cells.) Three of the eleven patients have died due to progressive disease. Complete blood counts on eight patients one year after infusion were completely normal, except one individual had a slight reduction in platelet counts ($103x10^9$/l).
February 22 2000	9701-173 Croop	**A Pilot Study of Dose Intensified Procarbazine, CCNU, Vincristine (PCV) for Poor Prognosis Pediatric and Adult Brain Tumors Utilizing Fibronectin-Assisted, Retroviral-Mediated Modification of CD34+ Peripheral Blood Cells with O^6-Methylguanine DNA Methyltransferase** **Update:** Notification of a missed safety test due to mis-communication. Appropriate tests were done subsequently.
From February 24 to May 16, 2000	9709-196 Smith and Dinauer	**Fibronectin-Assisted, Retroviral-Mediated Transduction of CD34+ Peripheral Blood Cells with gp91 phox in Patients with X-Linked Chronic Granulomatous Disease: A Phase I Study** **Updates:** Same issue concerning possible presence of replication competent retrovirus in transduced cells as for protocol 9701-173. See summary above.
February 24, 2000	9711-221 Crystal	**Phase I Study of Direct Administration of a Replication-Deficient Adenovirus Vector (Ad_{GV}VEGF121.10) Containing the VEGF121 cDNA to the Ischemic Myocardium of Individuals with Life Threatening Diffuse Coronary Artery Disease** **Amendment:** Trial has been amended to eliminate Groups B and C. Group B was a "compassionate use" cohort. Group C was for a blinded, controlled study of the highest safest dose determined in Group A of the trial vs. saline.
February 24, 2000	9804-243 Crystal *et al.*	**Phase I Study of Direct Administration of a Replication Deficient Adenovirus vector (Ad_{GV}VEGF121.10) Containing the VEGF121 cDNA to the Ischemic Lower Limb of Individuals with Peripheral Vascular Disease** **Amendments:** 1) Change from a one week interval between administration of Ad vector between patients to a one week interval between each dose escalation. 2) Elimination of adiluent-only (placebo) control group. Trial is now an open-label, dose-escalating study. 3) Length of follow-up has been changed from life-long to five years. 4) Elimination of transcutaneous oximetry as an efficacy test. Subsequent information leads one to suggest that the results are too variable to be of value for this study.
February 24, 2000	9806-258 Crystal	**Phase I Study of Direct Administration of a Replication Deficient Adenovirus Vector (Ad_{GV}VEGF121.10) Containing the VEGF121 cDNA to the Ischemic Myocardium of Individuals with Diffuse Coronary Artery Disease Via Minimally Invasive Surgery** **Amendment:** To add up to an additional 10 patients at a dose of $4x10^{10}$ particle units. Five of the patients will receive injections in two areas of ischemia and up to five will receive injections across the full left ventricle. This dose ($4x10^{10}$ particle units) has been used in protocol 9711-221.

February 24, 2000	9910-346 Stewart *et al.*	**A Phase II, Randomized, Multicenter, 26-Week Study to Assess the Efficacy and Safety of CI-1023 Delivered Through Minimally Invasive Surgery Versus Maximum Medical Treatment in Patients with Severe Angina, Advanced Coronary Artery Disease, and No Options for Revascularization** **Amendments:** Changes have been made to clarify requirements for some of the study procedures. In particular, if digoxin therapy is to be discontinued it must be done under the supervision of a cardiologist with the appropriate training.
February 28, 2000	9902-293 Kaufman	**Phase II Randomized Study of Vaccine Treatment of Advanced Prostate Cancer** **Amendments:** Clarifications have been made to the inclusion criteria in terms of tumor limited to the prostate, completed local therapy, and have an elevated PSA. Chemotherapy or hormonal therapy must have been completed at least six months prior to entry into this study; patient must have recovered fully from prior study. PSA levels must not have progressed on prior therapy.
February 28, 2000	9706-196 Smith and Dinauer	**Fibronectin-Assisted, Retroviral-Mediated Transduction of CD34+ Peripheral Blood Cells with gp91 phox in Patients with X-Linked Chronic Granulomatous Disease: A Phase I Study** **Amendments:** Administrative and clinical clarifications were made.
February 28, 2000	0001-370 Croop	**Gene Therapy for Patients with Fanconi Anemia: A Pilot Study** **Amendments:** Administrative and clinical clarifications were made.
February 29, 2000	9907-327/328/329 Isner and Chronos	**A Phase I Double-Blind, Placebo Controlled, Escalating Dose, Multi-Center Study of Ad2/Hypoxia Inducible Factor (HIF)-1a/VP16 Gene Transfer Administered by Intramuscular Injection to Patients with Critical Limb Ischemia Who are Not Candidates for Surgical or Percutaneous Revascularization** **A Phase I, Open-Label, Multi-Center Extension Study of Ad2/Hypoxia Inducible Factor (HIF)-1a/VP16 Gene Transfer Administered by Intramuscular Injection to Patients with Critical Limb Ischemia Who are Not Candidates for Surgical or Percutaneous Revascularization** **A Phase I, Open-Label, Single Dose, Roll-Over, Multi-Center Study of Ad2/Hypoxia Inducible Factor (HIF)-1a/VP16 Gene Transfer Administered by Intramuscular Injection to Patients with Critical Limb Ischemia Who are Not Candidates for Surgical or Percutaneous Revascularization** **Amendments:** Same amendments made to all of the above protocols. Amendments were made to clarify eligibility criteria and plasma VEGF levels, in addition to serum levels, will be measured at all pre-designated points. Procedure was developed for unblinding of a given patient to allow for the potential administration of the Ad vector in a "rescue procedure." Therefore, sponsor (Genzyme) in consultation with the investigators, independent eligibility reviewers, and data safety monitoring board chairman have developed of "treatment failure."
February 29, 2000	9907-328 Isner and Chronos	**A Phase I, Open-Label, Multi-Center Extension Study of Ad2/Hypoxia Inducible Factor (HIF)-1a/VP16 Gene Transfer Administered by Intramuscular Injection to Patients with Critical Limb Ischemia Who are Not Candidates for Surgical or Percutaneous Revascularization** **Amendment:** Specific to protocol 9907-328. Additional safety testing has been added to the extension sturdy to monitor for liver and immunological responses. In

		addition, a follow-up eye examination, at six months, has been added to monitor for any neovascularization
March 3, 2000	9906-323 Zarrabi *et al.*	**A Multi-Center, Open-Label, Randomized Study of the Safety and Efficacy of Multiple Intratumoral Injections of hIl-2 Plasmid (1.8 mg) Formulated with DOTMA/Cholesterol [Ratio 1:0.5 (-/+)] Liposomes in Patients with Unresectable or Recurrent/Refractory Squamous Cell Carcinoma of the Head and Neck** **Amendment:** Removal of methotrexate arm of study, due to patients withdrawing consent when randomized to non-gene transfer arm of the study.

March 3, 2000	9712-223 Brenner	**Phase I Study of Chemokine and Cytokine Gene Modified Allogeneic Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using a Retroviral Vector** **Update:** Notification that Baylor College of Medicine will be the only site for this study; St. Jude's is no longer a trial site.
March 3, 2000	9712-224 Brenner	**Phase I Study of Chemokine and Cytokine Gene Modified Autologous Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using an Adenoviral Vector** **Updates:** Notification that Baylor College of Medicine will be the only site for this study; St. Jude's is no longer a trial site. Release criteria have been corrected.
March 6, 2000	9808-263 Lang and Yung	**Phase I Trial of Adenovirus-Mediated Wild Type p53 Gene Therapy for Malignant Gliomas** **Amendments:** Changes in collection of samples for antibody testing and lumbar puncture and CSF sampling (if a fever develops) have been made.
March 6, 2000	9902-288 Schiller	**Phase I Pilot Trial of Adenovirus p53 and Radiotherapy on Non-Small Cell Lung Cancer** Eligibility criteria regarding radiation to the spinal cord were re-worded to clarify eligibility.
March 7, 2000	0001-382 Strother	**A Pilot Study of Gene Modified Autologous Neuroblastoma Vaccine for the Post-Chemotherapy Treatment of High Risk Neuroblastoma** **Amendment:** Release criteria have been corrected.
March 7, 2000	9712-223 Brenner	**Phase I Study of Chemokine and Cytokine Gene Modified Allogeneic Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using a Retroviral Vector** **Amendment:** Release criteria have been corrected.
March 8, 2000	9701-173 Croop	**A Pilot Study of Dose Intensified Procarbazine, CCNU, Vincristine (PCV) for Poor Prognosis Pediatric and Adult Brain Tumors Utilizing Fibronectin-Assisted, Retroviral-Mediated Modification of CD34+ Peripheral Blood Cells with O^6-Methylguanine DNA Methyltransferase** **Amendments:** Clinical clarifications were made.
March 8, 2000	9701-173	**A Pilot Study of Dose Intensified Procarbazine, CCNU, Vincristine (PCV) for Poor Prognosis Pediatric and Adult Brain Tumors Utilizing**

	Croop	**Fibronectin-Assisted, Retroviral-Mediated Modification of CD34+ Peripheral Blood Cells with O^6-Methylguanine DNA Methyltransferase** **Update:** Notification of a missed dose of CCNU due to a miscommunication
March 13, 2000	9904-304 Hurwitz	**Pediatric Phase I Study of AdV/RSV-TK Followed by Ganciclovir for Retinoblastoma** **Amendments:** Eligibility criteria for the first three patients has been modified to allow for patients with retinal detachment and vitreal seeding to be eligible. In addition, any patient who would be excluded from the study solely due to laboratory abnormalities may be included at the investigator's discretion.
March 14, 2000	9812-274 Comerota *et al.*	**A Phase I, Multi-Center, Open Label, Safety and Tolerability Study of Increasing Single Dose of NV1FGF Administered by Intra-Muscular Injection in Patients with Severe Peripheral Artery Occlusive Disease** **Amendments:** Patients may be recruited with a positive PSA test if a prostate biopsy is negative for the presence of a tumor. Creatinine and bilirubin levels will no longer be measured. To date, no renal or liver toxicities have been observed in either animals or patients. In addition, serum VEGF levels will be measured in all patients treated with FGF. FGF is a known inducer of VEGF expression. No additional blood will have to be drawn for VEGF analysis.
March 14, 2000	9810-268 Antonia	**Treatment of Patients with Stage IV Renal Cell Carcinoma with B7-1 Gene-Modified Autologous Tumor Cells and Systemic IL** **Update:** From January 1999 to February 2000, 20 patients were enrolled in the trial and 13 completed the course of treatment. Four patients were enrolled in dose levels one and three and five patients enrolled in dose level two. Sufficient cells were not generated for three patients; however, these patients requested and received the vaccine at a lower dose. Three of the 13 patients have died due to progressive disease. Eleven of the 13 patients had lesions that were evaluable for a response. One of the 11 had a partial response, one a minor response, and one patient had stable disease. As of this date, three patients have not been re-staged.
March 15, 2000	9701-173 and 0001-370 Croop	**A Pilot Study of Dose Intensified Procarbazine, CCNU, Vincristine (PCV) for Poor Prognosis Pediatric and Adult Brain Tumors Utilizing Fibronectin-Assisted, Retroviral-Mediated Modification of CD34+ Peripheral Blood Cells with O^6-Methylguanine DNA Methyltransferase** **Gene Therapy for Patients with Fanconi Anemia: A Pilot Study** **Update:** Received a copies of assurance letters from Dr. Croop to Amgen (supplier of essential reagents for these two trials) indicating that these trials are being conducted according to all government regulations and guidelines and are in full compliance with good clinical practices and the Code of Federal Regulations.
March 16, 2000	0001-386 Antonia	**Phase II Study of a B-7.1 Gene Modified Autologous Tumor Cell Vaccine and Systemic IL-2 for Patients with Stage IV Renal Cell Carcinoma** **Amendments:** Based on an analysis of the phase I trial, the lowest dose level of transduced cells will be used in the phase II trial. This is based on the fact that there was no significant difference among the three dose levels in the phase I trial in terms of toxicity, immunogenecity, and clinical response. A provision for the administration of fewer than the target number of cells has been included. Vaccine cells for approximately 10% of the patients in the phase I study

		were not generated in specified numbers. These patients still requested that they receive the vaccine. A dose reduction scheme has been included for patients who experience excessive toxicity from interleukin-2.
March 16, 2000	0001-369 DeAngelo	**A Phase I Study of Vaccination with Lethally Irradiated, Autologous Acute Myeloblastic Leukemia Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor in Patients with Advanced Myelodysplasia or Acute Myelogenous Leukemia** **Update:** Due to a production delay at the Harvard Institute of Medicine, this trial has been initiated with vector produced by CellGenesys.
March 20, 2000	9712-224 Brenner	**Phase I Study of Chemokine and Cytokine Gene Modified Autologous Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using an Adenoviral Vector** **Amendments:** Patient eligibility has been clarified to note that patients who would be excluded due solely to laboratory abnormalities may now be included at the investigator's discretion. Adverse event reporting has been clarified. Vector release specifications have been added.
March 20, 2000	0001-382 Strother	**A Pilot Study of Gene Modified Autologous Neuroblastoma Vaccine for the Post-Chemotherapy Treatment of High Risk Neuroblastoma** **Amendments:** Patient eligibility has been clarified to note that patients who would be excluded due solely to laboratory abnormalities may now be included at the investigator's discretion. Adverse event reporting has been clarified.
March 20, 2000	9712-223 Brenner	**Phase I Study of Chemokine and Cytokine Gene Modified Allogeneic Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using a Retroviral Vector** **Amendments:** Patient eligibility has been clarified to note that patients who would be excluded due solely to laboratory abnormalities may now be included at the investigator's discretion. Adverse event reporting has been clarified.
March 21, 2000	9905-319 Brenner	**Treatment of High Risk Acute Leukemia with CD40 Ligand and IL-2 Gene Modified Autologous Bone Marrow Fibroblasts and Tumor Cells** **Amendments:** HLA typing has been added to assist in the analysis of the immune response after vaccination. Follow-up has been modified to indicate that not more than 5ml/kg of peripheral blood will be drawn (maximum 20ml for children, 40ml for adults), prior to each vaccine administration, at weeks four and ten, then monthly for one year, then annually for ten years. Adverse event reporting has been modified.
March 23, 2000	9804-237 Roth	**A Phase I Safety Study of Autologous Transfected Human Fibroblasts Producing Human Factor VIII in Patients with Severe Hemophilia A** **Update:** Notification from the sponsor, Transkaryotic Therapies, that all gene transfer trials at the Beth Israel Deaconess Medical Center were being placed (as of February 4) on "hold." On February 18, the principal investigator was notified that the study could

		be resumed.
March 24, 2000	9902-284 Ragni *et al.*	**Phase I Multi-Center, Single Treatment Dose Escalation Study of Factor VIII Vector [HFVIII(V)] for Treatment of Severe Hemophilia A** **Update:** Correspondence from sponsor (Chiron) indicating that trial has been placed on clinical hold by the FDA. A single positive PCR reaction for the presence of viral vector in a semen sample from one patient was observed. A repeat of the assay using a fresh DNA from the same sample and DNA from a new sample were both negative. Conclusion from Chiron is that the initial positive result was a false positive due to contamination.
March 29, 2000	9902-290 Albertini	**Phase I Trial of Immunization Using Particle-Mediated Transfer of Genes for GP-100 and GM-CSF into Uninvolved Skin of Patients with Melanoma.** **Update:** Notification that trial is closed to new enrollment due to the presence of a 109 bp sequence in both plasmids homologous to the *nef* gene of Simian Immunodeficiency Virus. More detailed information is present in the FYI section of the RAC meeting materials.
April 12, 2000	9901-281 Haluska	**Phase I/II Trial of the Safety, Immunogenicity, and Efficacy of Autologous Dendritic Cells Transduced with Adenoviruses Encoding the MART-1 and gp100 Melanoma Antigens Administered With or Without Low Dose Recombinant Interleukin-2 (rIL-2) in Patients with Stage IV Melanoma** **Amendments:** Two changes in the inclusion criteria: 1) Patients no longer have to be HLA-A2 +; only antigen positive regardless of HLA type; and 2) enrolled patients do not have to have a measurable lesion of at least one centimeter in the longer diameter. Melanoma metastases only a few millimeters in size are easily evaluated.
April 13, 2000	9804-250 Swisher	**An Efficacy Study of Adenoviral Vector Expressing Wildtype p53 (Ad5CMV-p53) Administered Intralesionally as an Adjunct to Radiation Therapy in Patients with Non-Small Cell Lung Cancer** **Amendments:** Doses of vector will now be given in particles as opposed to plaque forming units. Tests performed to measure vector distribution have been eliminated due to completion of an analysis of similar tests on a similar patient population from previous studies.
April 19, 2000	9709-196 Smith and Dinauer	**Fibronectin-Assisted, Retroviral-Mediated Transduction of CD34+ Peripheral Blood Cells with gp91 phox in Patients with X-Linked Chronic Granulomatous Disease: A Phase I Study** **Update:** To date two patients have been enrolled in this trial (both in 1999; trial was open to accrual in 1997).
April 19, 2000	0001-370 Croop	**Gene Therapy for Patients with Fanconi Anemia: A Pilot Study** **Update:** Notification that investigator is aware of the new maximal dose of colony stimulating factor (CSF). The informed consent has been modified to reflect possible life-threatening allergic reactions to CSF.
April 25, 2000	9712-224 Brenner	**Phase I Study of Chemokine and Cytokine Gene Modified Autologous Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using an Adenoviral Vector** **Amendments:** Patient eligibility has been clarified to note that patients who would be excluded due solely to laboratory abnormalities may now be included at the investigator's discretion after approval by the Center for Cell and Gene Therapy Protocol Review Committee (at Baylor) and the FDA. Eligibility criteria modified to state that sexually active patients must be willing to use

		appropriate birth control methods during and for three months after completion of the study.
April 25, 2000	0001-382 Strother	**A Pilot Study of Gene Modified Autologous Neuroblastoma Vaccine for the Post-Chemotherapy Treatment of High Risk Neuroblastoma** **Amendments:** Patient eligibility has been clarified to note that patients who would be excluded due solely to laboratory abnormalities may now be included at the investigator's discretion after approval by the Center for Cell and Gene Therapy Protocol Review Committee (at Baylor) and the FDA. Eligibility criteria modified to state that sexually active patients must be willing to use appropriate birth control methods during and for three months after completion of the study.
April 25, 2000	9712-223 Brenner	**Phase I Study of Chemokine and Cytokine Gene Modified Allogeneic Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using a Retroviral Vecto** **Amendments:** Patient eligibility has been clarified to note that patients who would be excluded due solely to laboratory abnormalities may now be included at the investigator's discretion after approval by the Center for Cell and Gene Therapy Protocol Review Committee (at Baylor) and the FDA. Patients must be willing to practice birth control during the study and for six months after completion of the study. Adverse event reporting has been modified.
May 2, 2000	9910-350 Alberts and Gershenson	**A Phase I Dose Escalation Study of Intraperitoneal E1A-Lipid Complex (1:3) with Combination Chemotherapy in Women with Epithelial Ovarian Cancer** **Amendments:** Concerning a redefinition of the dose limiting toxicity and administration based on the redefinition. Also, clarification of the observational period patients receiving a given dose and before administration to patients in the next cohort.
May 8, 2000	9705-187 Hall	**Phase I Trial of Adenoviral-Mediated Herpes Simplex Thymidine Kinase Gene Transduction in Conjuction with Ganciclovir Therapy as Neo-adjuvant Treatment for Patients with Clinically Localized (Stage T1c and T2b&c) Prostate Cancer Prior to Radical Prostatectomy** **Amendment:** Addition of an intermediate dose of $3.3x10^{11}$ plaque forming units between the $1x10^{11}$ and $1x10^{12}$ doses. This will increase the total number of patients in this protocol to 12.
May 8, 2000	9711-221 Crystal	**Phase I Study of Direct Administration of a Replication-Deficient Adenovirus Vector (Ad_{GV}VEGF121.10) Containing the VEGF121 cDNA to the Ischemic Myocardium of Individuals with Life Threatening Diffuse Coronary Artery Disease** **Amendment:** Follow-up yearly for five years has been amended to a follow-up at one year only.
May 8, 2000	9804-243 Crystal *et al.*	**Phase I Study of Direct Administration of a Replication Deficient Adenovirus vector (Ad_{GV}VEGF121.10) Containing the VEGF121 cDNA to the Ischemic Lower Limb of Individuals with Peripheral Vascular Disease** **Amendment:** Follow-up yearly for five years has been amended to a follow-up at one year only.
May 8, 2000	9806-258 Crystal	**Phase I Study of Direct Administration of a Replication Deficient Adenovirus Vector (Ad_{GV}VEGF121.10) Containing the VEGF121 cDNA to the Ischemic Myocardium of Individuals with Diffuse Coronary Artery Disease Via Minimally Invasive Surgery** **Amendment:** Follow-up yearly for five years has been amended to a follow-up at one

		year only.
May 8, 2000	9908-333 Swindells	**A Multicenter Evaluation of the Safety and Efficacy of Hematopoietic Stem Cells Transduced with RevM10polAS (RevM10polAS HSCIP) as Therapy for HIV-1 Infected Persons** **Amendments:** Number of changes have been made to clarify various aspects of the protocol. Results from a previous study indicate that a lower dose (1.8g/m^2 vs. 2.4g/m^2) of cyclophosphamide is as effective as the dose initially proposed. Engraftment of hematopoietic stem cells will be measured at 28 rather than 60 days.
May 10, 2000	9906-322 Tuszynski	**A Phase I Study of NGF Ex Vivo Gene Therapy for Alzheimer's Disease** **Amendment:** Amendment submitted to the FDA to lower the minimum age from "... 60 to 50 with a diagnosis of probable Alzheimer's Disease of mild severity." Rationale behind the change is that a large number of patients over the age of 50 have been screened, but to date none have meet the full inclusion criteria.
May 12, 2000	0002-391 Thompson *et al.*	**Phase II Study of Leuvectin in Patients with Metastatic Renal Cell Carcinoma** **Amendments:** Measurement of total tumor burden changed to measurement of up to five indicator lesions. Patients are now allowed to remain on study after the first cycle with disease progression (unless the progression is determined to be clinically significant). Purpose is to allow patients who experience initial progression to remain on study. Patients will not be removed from the study due solely to disease progression (a 25% increase in tumor area) after the first cycle. Inclusion criteria modified to allow patients with a performance status of 0 with three organs with metastatic disease (instead of two or fewer) to be enrolled. In addition, patients with tumors of pure papillary and transitional cell types are excluded.
May 12, 2000	9910-346 Stewart *et al.*	**A Phase II, Randomized, Multicenter, 26-Week Study to Assess the Efficacy and Safety of CI-1023 Delivered Through Minimally Invasive Surgery Versus Maximum Medical Treatment in Patients with Severe Angina, Advanced Coronary Artery Disease, and No Options for Revascularization** **Amendment:** Patients with Canadian Cardiovascular Society (CCS) Class II are now eligible for the study as long as they meet all of the other requirements. Classification under the CCS system is subjective and is not a primary study end-point.

May 17, 2000	9911-358 and 9911-359 Sung and Woo	**Phase I Trial of Adenoviral Vector Delivery of the Human Interleukin-12cDNA by Intratumoral Injection in Patients with Metastatic Breast Cancer to the Liver** **Phase I Trial of Adenoviral Vector Delivery of the Human Interleukin-12cDNA by Intratumoral Injection in Patients with Primary or Metastatic Malignant Tumors in the Liver** **Amendments:** Study has been amended based upon the comments at the March 2000 RAC discussion and the follow-up letter from OBA. Specifically the investigators have: 1) Patients with primary liver neoplasms are no longer eligible for participation in protocol 9911-359. 2) Hepatic resection is included as a possible alternative in the informed consent document.

		3) Dr. Warren (UCSF) has been contacted to set-up an appointment to discuss hemodynamic monitoring catheters (Swan-Ganz).
May 22, 2000	9706-196 Smith and Dinauer	**Fibronectin-Assisted, Retroviral-Mediated Transduction of CD34+ Peripheral Blood Cells with gp91 phox in Patients with X-Linked Chronic Granulomatous Disease: A Phase I Study** **Amendments:** Administrative and clinical clarifications were made.
May 24, 2000	9902-287 Schiller and Carbone	**Phase I Pilot Trial of Adenovirus p53 in Bronchioloalveolar Cell Lung Carcinoma (BAC) Administered by Bronchoalveolar Lavage** **Amendment:** Dose modification information has been corrected to clarify that recovery is necessary to grade II or less for those pulmonary toxicities that have not have a defined grade I toxicity.
May 31, 2000	9910-352 Belldegrun and Klein	**Phase I/II Study Evaluating the Safety and Efficacy of Leuvectin Immunotherapy for the Treatment of Locally Recurrent Prostate Cancer Following Radiation Therapy** **Amendments:** Minor amendments have been made, including collection of survival data every six months. Patients with a PSA of at least 1.0ng/ml are now eligible for the study.
May 31, 2000	9905-312 Belldgrun and Klein	**Phase II Study Evaluating the Safety and Efficacy of Neoadjuvant Leuvectin Immunotherapy for the Treatment of Prostate Cancer** **Amendments:** Minor amendments have been made, including collection of survival data every six months. Patients with a PSA of at least 1.0ng/ml are now eligible for the study.
June 12, 2000	9906-322 Tuszynski	**A Phase I Study of NGF Ex Vivo Gene Therapy for Alzheimer's Disease** **Amendment/Update:** Exclusion criteria have been changed to allow enrollment of patients who have been cancer-free for 18 months as opposed to five years. Notification that Dr.Tuszynski has a financial interest in a company to develop gene therapy for neurological disorders. This company is not providing financial support for protocol 9906-322. More information is present in the FYI section of the RAC meeting materials.